ملخص

pharmacology

Introduction and ANS

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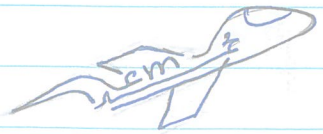
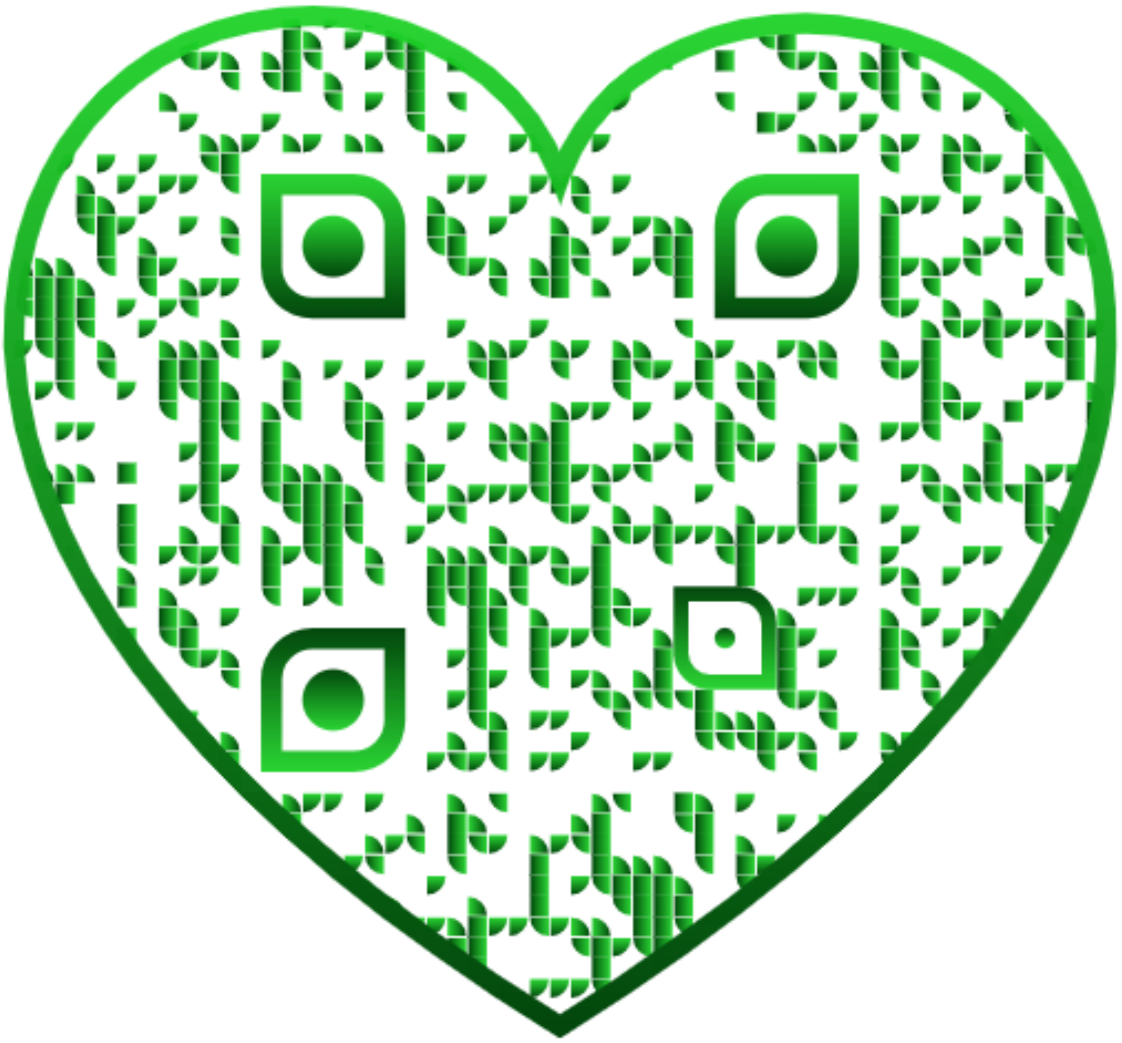


مع تحيات
اللجنة العلمية في الدفعة 35 طب بيشة



2020

1st Lecture

General Pharmacology

Pharmacology: is the science of drug

What is the drug: any substance which can alter, treat, Diagnose or prevent disease

Treating → Paracetamol

Prevention → Vaccine

Diagnosis → naloxone for Heroine addiction

→ Edrophonium for myasthenia G.

Sources of drug

Neutral

- From plant → Atropin & hyoscine
- From animal → insulin & heparin
- From microorganism → penicillin
- From marin → Fish liver oil
- From soil → minirals ((Zn))

Synthetic

- Represent 90 %
- low coast
- e.g Aspirin

Route of administration

- parentral ((iv - id - im - sc))
- oral
  - solid ((tablet))
  - liquid ((sera))
- topical
  - cream
  - drops
  - ointment
- inhalation
  - general
  - asthma

sciences of drug

Pharmacokinetic : is the effect of body on drug

Pharmacodynamic : is the effect of drug on the body

Therapeutic use : is the proper choice of drug with proper dose for each situation.

Toxicology : is the study of drug toxicity which include identification of :

- Toxic dose
- symptom of toxic dose
- Antidote.

Note not all drugs overdose are toxic

In pharmacodynamic you should to know:

A : mechanism of action «MOA» B : Pharacological action

- Receptor —(through / e.g)→ Adrenalin
- Enzyme —(e.g)→ Aspirin through cyclo-oxygenase
- Ion channel —(e.g)→ Lidocaine
- DNA —(e.g)→ «Anti-viral Drug» mitronidazol
- Chemical reaction —(e.g)→ Antacid «HCO_3» For neutralization
- physical reaction → sucralfate to treat peptic ulcer; charchol to oppose toxic dose taken
- cell wall —(e.g)→ «Anti-Fungal drug» penicillin

Pharmacological Action

Clinical use — side effect

Side effect include:

1- **Tolerance**: is one type of misuse of drug which charactrize by ↑ the dose of drug to get the same effect fo same disease. e.g. using paracetamol for treating h dache after long time you should take more ta to get the same effect.

2- **Tachyphylaxis**: is the rapid occurance of tolerance

3- **Dependent**: is severe state of craving in which sudo stop of drug uses may cause central withdr effect e.g Diazepam.

4- **Addiction**: is severe state of craving in which sud stop of drug use may cause central & perep withdrawal effect. e.g. morphin & Heroin. which lead to many symptom may end by dea

5- **Idiosyncrasy**: unusual or unexpected side effect of dr due to genetic variation e.g penicillin which cause hypersensitivity reaction.

2nd Lecture

Pharmacokinetics

Pharmacokinetics: is the effect of body on the dru
which include

1. Absorption
2. Distribution
3. Metabolism
4. Excretion

1) Absorption: Transfer of drug from site of administra
to the systemic circulation

Factor affect absorption:-

A: Factor related to drug:

1- solubility: « Lipid soluble sub. more absorped tha
water soluble substance »

2- particle size: « particles will small size is more a
ped than particles with large size.

3- physical propertize « solid - liquid - gas »
« liquid is the best »

4- Ionization: « ↑ polarity ⟶ ↓ absorption

5- dosage form: « taplet - capsule - spray - drop -

B: Factor related to the patient.

1- Route of administration « entral - topical --- etc »

2- Health state e.g constipation ⟶ ↑ absorption

vomiting & diarrhea ⟶ ↓ absorp

3- Blood Flow

4- presence of food in GIT ⟶ ↓ absorption

Biovailability: is the Fraction of dosed drug that reach

blood circulation = $\frac{\text{conc. of drug in blood}}{\text{dose of drug}}$ x

> 80% excellent absorption < 50% poor absorption

e.g: drug dose 500 mg while the amount that absorped is 300 mg

Biovailability = $\frac{300}{500} \times 100 = 60\%$

good absorption

2) Distribution: Leaving of drug From systemic circulal to interstitial space of all tissue in the bo

Drug found in Blood circulation in 2 form

Binding Form « inactive » Free Form « active

« Bind to plasma protein mainly albumen »

3) Metabolism: «the First step of drug elemination »
« is chemical modification of drug structure

- conversion of drug from Lipid soluble to water soluble be easily excreted «from active to inactive»
- Convertion of drug From inactive ⟶ active «prodrug» e.g Enalapr
  Active ⟶ Active metabolite e.g Diazepa
  Active ⟶ toxic metabolite e.g paracet
  But in chronic use

Factor affect drug metabolism:

★ health state of liver
★ Age « Enzymes more active in young people»
★ Sex « metabolic Rate in male is hieghe than that in Female
★ Drug-Drug interaction

- metabolic inducer
«drug stimulate metabolism»
E.g «rifampin-phenytoin»
whenwe use them with warfarin ⟶ ↓ its action
الدواء يسبب زيادة الجرعة وإما في الفصل بينهما

- metabolic inhibitors
«drugs inhibit metabolism»
E.g «erythromycin - Ritanovi
when we use them with warfarin ⟶ ↑ its effect
الدواء يسبب تقليل الجرعة وإما في الفصل بين الدوائين

4) Excretion: removal of drug outside the body. depend on healthy state of kidney and liver.

* Agonist: drug which bind to receptor and produce biological responce: e.g Adrenergic agonist: drug which bind to adrenegic receptor and produce effect similar to that produced by natural neuro-transmitter (adrenalin- nor-adrenalin -Dopamin)

* Antagonist: drug which bind to receptors to decrease or oppose effect of another drug or endogenous ligand e.g adrenergic antagonist drug which bind to adrenergic receptor and produce opposite effect to that produced by natural neurotransmitter.

Therapeutic indix (TI): is the degree of drug safiety

$= \frac{\text{Toxic dose 50}}{\text{effective dose 50}} = \frac{TD\,50}{ED\,50} =$

كلما قلت الـ TI كلما كان الدواء غير آمن

E.g. Drug A: TD50 = 50mg ED50 = 20gm

$TI = \frac{20000}{500} = 40$

* Potency: « the strength of drugs » فعالية الدواء
* Efficiency: maximum responce produced by drugs

- if we have two drugs A = 5 mg B = 100 mg with the same efficiency. drug A will be more potent due to concentration of drug.
- if we have two drugs A = 10 mg B = 10mg But A: wit high efficiency A will be more efficient.

onest of action of drug: is the duration between admi -ration and appearance of effect of

Duration of action of drug: is the time between onest and end of action of drug.

Estemation of drug responce.

1. disappearance of symptom of disease
2. measuring of parameters مثل قياس نسبة السكر في الدم
3. drug concentration in blood

3rd Lecture

Drug Affecting ANS

هذه المقارنة لم يشرحها الدكتور وإنما نوه عليها فقط:

Tissue or organ	sympathetic	parasympathetic
• CNS	• excitement - learning (α-and-β)	• Resting - memory (M_4 & M_5)
• Eye	• mydriases α_1	• miosis
	• Relaxation of ciliary m β_2	• contration of ciliary
	• ↑ secretion of aqueous homer fluid (B_2)	• ↑ drinage of aque homer Fluid
• salivary gland	α_1 trophic secretion	profuse watary secretion (M_3)
• heart	↑ all cardiac properitive (β_1)	↓ all cardiac properti (M_2)
• Blood vessels	V.C of most B.V (α_1)	
	V.D of coronary & B.V in Skeletal muscle (B_2)	
• GIT	relaxation of wall (B_2)	Contraction of wall (M_3)
	contraction of sphencter (α_1)	Relaxation of spheric (M_3)
• Lung	Bronchodilatation (B_2)	Bronchoconstriction (M_3)
	↓ Bronchial secretion (α_1)	↑ Bronchial secreti (M_3)
• U.B	relaxation of wall	contraction of wall
	contraction of sphencter	Relaxation of sphinc
Genetal organ	male Ejaculation	Erection of penis
	Female contraction / Relaxation of uterus (α_1 / B_2)	Erection of clitor

Drug affecting ANS

* Parasympathomimetic drug — Direct / indirect
* Parasympatholytic drug

	Parasympathomimetic drug	
classification	Direct	indirect
Examples	pilocarpine	• pyridostigmine • Rivastigmine
MOA	direct stimulation of muscarinic receptor	by inhibition of Ach-esterase enzyme
pharmacological action	similar to Ach	
side effect	* Bradycardia * hypotension * salivation * diarrhea * dyspepsia * abdominal cramps	* miosis * Frequecy of urinat * Bronchoconstrictio

clinical use

1] Glaucoma « ↑ intraocular pressure » we use pilocarp
as eye drop « ↑ drinage of aquous humer Fluid »

2] Sjögren syndrom « is an autoimmune disease in whic
the body Form antibodies against lacrimal & salivar
gland » we use pilocarpine and cevimeline

3] myasthena gravis « autoimmune disease in which the b
Form antibodies against nicotinic receptor in neuron
cular junction »

ثم تشخيصها عن طريق الطلب من المريض أن يعد الى ٥٠ في البداية
ون نبرة صوتية قوية ومن ثم تبدأ بالخفوت تدريجياً

Fatiguability ← الكلمة الوحيدة التي يومن بها المرض
treated by « Neostigmins & pyridostigmine.

4] Lambert - eaton syndrom « is an autoimmune disease
which the body Form antibodies against voltage gateo
Ca^{+2} channel in presynaptic neuron which lead to ↓ release A
تختلف عن myasthena gravis أن الحركة تبدأ بطيئة ومن ثم تزداد
تدريجياً
treated by « pyridostigmine »

5] ALzheimer disease « loss of recent memory in elderageo
Treated by → Rivastigmine.

- contraindication:

  ✱ Asthma ✱ urinary track obstruction ✱ peptic ulce

Acetylcholine lacks therapeutic importance. why?

Due to ✱ its multiplicity of action leadin to diff
effect « Not specific »

✱ its rapid inactivation by the cholinestera

Parasympatholytic « Anti-cholinergic = anti-muscarinic »

- Examdex ✱ Atropine
  ✱ Hyoscine
  } Alkaloid derived from plant

- side effect:

1- Loss of recent memory «amnesia»
2- mydriasis - cycloplegia «paralysis of ciliary muscle
3- dry mouth → « الدريعن يتعرقش من الحنوك لساطع
4- dry skin Atropine-like side effect
5- tachy cardia
6- constipation
7- urine retention

- contraindication
  - ★ glaucoma ((because it ↓ drinage of aquous Homer fluid))
  - ★ Benign prostatic hyperplesia ((BPH))

Note benign tumer in prostate found in transitional zone whe
malignant tumer found in perephral zone.

- clinical use
  1. Non-infectious diarrhea
  2. severe bradycardia
  3. irreversable Ache~~se~~ → esterase inhibitors poisoning:

     these organophosphorus compound which found in:

     Nerve gases : sarin & soman

     insecticide : Malathion & parathion

     ((these compound inhibit Ach esterase enzyme by irre
     sable mechanism which lead to ↑ acetyl cholin an
     produce more longer parasympathetic Action as:

     - convulsion
     - Bradycardia → cardiac arrest
     - Bronchoconstriction
     - Frequency urination
     - Diarrhea

All these symptom treated by atropin except convulsi

why? Because convulsion occur in skeletal muscle which ha
nicotonic receptor whereas Atropin is antimuscarinic drug

4] Bronchial asthma «Ipratropium»

5] Paskinson's disease « neurological disease caused by decr
dopamine or increasing acetylcholin in basal ganglia.
treated by « procyclidine & Benztropine»

6] in operation inorder to ↓ secretions

7] ophthalmological use « for eye examination and treati
inflammation in iris ~~and~~ choroid, and ciliary body
treated by Atropin or tropicamid

8] urinary incontinence.

P20 | |

4th Lecture

Drug affecting SNS

Sympathomimetic Drug

Direct	in direct
these drug stimulate Adrenergic receptor directly	these drug stimulate release of chatecolamin from presynapti neurons

- α-B agonist
- α agonist
- B agonist
- D agonist

- Examples: adrenaline - Dopamine — Amphetamine
- clinical use of sympathomimetic drug:

1) Hypotension and shock

* in cardiogenic shock
  - Dopamine → act on D, α, B depend on the dose
  - Adrenaline (الترتيب حسب الأفضلية)
  - Nor-adrenalin

Dobutamine also used for treating cardiogenic shock

* in hypovolemic shock we use nor-adrenaline mainly
* In anaphylactic shock we use adrenaline mainly
* Phenylephrine (pure α1 agonist) use in vascular shock

we use adrenaline in anaphylactic shock due to it is a physiological anagonist for histamin its dose [0.5 – 1 Taken I.M. or I.V.]

2) Decongestion for (eye - sinuses - nose - Respiratory) Congestion ("vasodilatation")

we use these drug:

* pseudoephedrine
* oxymetazoline
* xylometazoline
* tetrahydrozoline
* Phenylephrine

3) Bronchial asthma

* salbutamol ("Albuterol") } taken by inhalation or injectio
* Salmeterol
* metaproternol

4) prevention of premature labor

* salbutamol ("albuterol") —▷ relaxation of uterus

5) Acute heart Failure

* dobutamine
* dopamin. we do not use Nor-adrenaline due t
* adrenalin it lead to Reflex Brady cardia.

6) with local anesthetic drug ("adrenalin") why?

Because its v.c effect which prolongate the effect of anesthetic drug by 3 mechanism.

1- ↓ systemic circulation «localization of drug»

2- ↓ Bleeding

3- ↓ side effect of drug.

7) ADHD «Attention deficit hyperactivity disorder»

هذا المرض غالباً ما يصيب الأطفال . حيث أن الطفل المصاب يكون نشط بدنياً لأبعد الحدود وكذلك أيضاً بليد ذهنياً لأبعد الحدود

treated by → methylphenidate.

«amphetamine derivative»

Other drug

methyldopa
clonidine
apraclonidine
Tizanidine

these drug stimulate α_2 receptor in presynaptic neuron and ↓ releasing neuro-transmitter to synaps.

- methyldopa is safe drug for gestational hypertensio

Mechanis of action → α_2 agonist

→ ~~per~~ inhibit ehatecolamin formation «by formation of false neurotransmitter

methyldopa → methyldopamin → methyl-nor-adren

methyl adrenaline ←

- clonidine used for treating ✱ hypertension
  ✱ Addictive symptom after withdrawa
- apraclonidine for treating Glaucoma
- Tizanidine used for treating Spasticity.

LMNL ("lower motor neuron lesion") ⟵ ل ارتخابي

UMNL ("upper motor neuron lesion") ⟵ ل تشنجي

علاج منوم ~~كان~~ صنع بواسطة شركة ألمانية كان يستخدم Thalidomide
~~بكثرة~~ بكثرة في القرن الماضي ولكن وجدوا أنه يسبب تشوهات في الأجنة
حيث أن الأطفال كانوا يولدوا بدون أطراف « Amelia » أو بأطراف حرفية

Are you pregnant or lactating? سؤال هم قبل وهن الدواء

تقسيم الأغذية والأدوية التي تعطى للمرأة الحامل الى ستة مجموعات

Group A Foods لا تأثر على الحمل ولا على الجنين

Group B some drug « penicillin - methyldopa - paracitamol »

Group C علاجات لا تأثر على الجنين

Group D

Group E

Group X ١٠٠٪ علاجات تؤثر على الحمل وتسبب تشوهات في الجنين بنسبة

propranolol does not used for patient with asthma

Side effect of sympathomimetic drug.

A: Direct sympathomimetic drugs.

- **Adrenaline**
  - hypertension
  - palpitation
  - tachycardia
  - arrhythmia
- **Nor-Adrenaline**
  - hypertension
  - reflex Bradycardia
  - not much tachycardia
- **Salbutamol**
  - hyperglycemia
  - tremor in «tongue & extrimeties»
  - not much tachycardia
- **Dobutamine**
  - tachycardia
- **Dopamine**
  - tachycardia
  - hypertension
  - nausia
  - vomiting

B: Indirect sympathomimetic drug

- ↑ ABP
- Tachycardia
- Constipation
- urinary retension
- mydriasis

} peripheral

Euphoria & Relive of Fatigue followed by:

- depression
- anxiety
- insomnia
- Phopia
- tolerance على المدى البعيد

} centrally

- Contraindication:
  - hypertension
  - cardiac arrhythmias

- Drug interaction

MAOI (mono-Amino-oxidase inhibitor) e.g. tranylcypromine which ↑ catecholamin and lead to many effect

→ hypertension crisis

→ organ damage

5th Lecture

Drugs Affecting SNS

Sympatholytics:

- classes
  - α- Blockers
  - β- Blockers
  - α_2- Agonist
  - storage inhibitors

- α-Blockers
  - A: Non selective α-Blaker «phenoxybenzamine »
  - B: selective α-Blaker . « Prazosin -tamsulosin »

- therapeutic use of α-Blockers
  1. hypertension «prazosin» on α_1
  2. Benign prostatic Hyperplesia «BPH»
     which charactrized by
     - hesitancy of urination
     - weak urine flow
     - uncomplete emptying of U.B

     treated by Tamsulosin which act on α_{1A} and lead to relaxation of neck of U.B & prostate

3] Pheochromocytoma ((10 % tumer))

tumer in suprarenal ~~medulla~~ medulla. which lea

to ↑ secretion of ~~cate~~catecholamine

~~the~~ skin is pale due to V.C effect of adre

Treated by phenoxybenzamin & propanolol

4] Raynaud's diseaseasr

((vascular disease which cause numbness & cyano

of the Fingers and toes.

Treated by phenoxybenzamin. But Ca^{++} channel b

is better.

■ side effect of α- Blockers.

* postural hypotension
* Reflex tachycardia ((more with phenoxybenzam

less with prazosin and least with tamsulosin))

* nasal stiffness ((congestion))
* myosis الدواء لا يستطيع الرؤية في الجنود الخائفت

■ Contraindication of α-Blocker:

Hypotension

- classification: B-Blocker
  - selective
  - non-selective
- example
  - selective: ★ atenolol B_1; ★ metoprolol B_1; ★ Bisoprolol B_1; ★ betaxolol B_1; ★ Butoxamin B_2 (more used clinically)
  - non-selective: ★ propranolol; ★ nadolol; ★ timolol; ★ pindolol

- clinical use of B-Blocker
  1. Hypertension through inhibit B_1 in heared which ★ all heart propertize and B_1 in Kidney ★ renin
  2. Angina pectoris
  3. Cardiac arrhythmia
  4. hyperthyrodism (propranolol Better than other dr
  5. Glaucoma (timolol & nadolol)

     Drug used for treating glaucoma:-
     - ★ pilocarpine
     - ★ apradonidin
     - ★ CAI (carbonic anhydr) (dorsolami
     - ★ prostaglandin
     - ★ B-Blocker
  6. prophylaxis of migrain: (propranolol) How ?
     unknown (through retrospective studies)

7] congestive heart failure

« Bisoprolol - Metoprolol - Carvidolol »

8] anexiety

9] portal hypertension

« propranolol but in acute state other drug used »

side effect of B-Blocker.

- Bradycardia
- Bronchoconstriction
- hypoglycemia
- cold extrimeties
- Fatigue

contraindication of B-Blocker

- Asthma
- severe bradycardia
- vasospastic angina
- perepheral vascular disease

Drug interaction.

Ca^{+2} channel blocker which found in B.V & heart e.g. Diltiazem, verapami

α_2 - Agonists. قد سبق شرحهم

e.g methyldopa

side effect of methyldopa

- ✲ Depression
- ✲ hypertension
- ✲ Bradycardia
- ✲ Parkinson's disease
- ✲ hyperprolactinemia
  - Gynecomastia in Male
  - Disturbances in menstrual cycle in Female

storage inhibitor

Reserpine « Alkaloid drug which inhibit storage of catecholamin so that they degraded by MAO

why catecholamin stored in vesicle ?

in order to protet them fom MAO & COMT

- therapeutic use
  - in hypertension
  - in psychosis « side effect of amphetamine »